

# Radiation of Pelvic Malignant Disease

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IN CONSIDERING any such topic as the radiation therapy of pelvic malignant disease, it is well to start by acknowledging two facts: First, that the therapeutic use of irradiation is still involved in the management of the overwhelming majority of pelvic malignant lesions and, second, that the age of the isotope is permanently with us from the point of view of therapy. The conclusion from these two premises is that we have been thrust into the position of having a considerable number of new agents and modalities with which we must, of necessity, become acquainted from the point of view of their limitations and potentialities. Our situation is not unlike that of the internist who originally had only regular insulin available for diabetic patients, and suddenly acquired protomine zinc insulin and a wide variety of other therapeutic weapons. Each of these had in common the ability to control the blood sugar, yet each has distinct differences, and various combinations of the available agents are indicated for various individual patients.

Many of the new sources of irradiation cannot as yet be judged from the point of view of their final results. Actually, however, there is no great reason at present to assume that the new sources of irradiation will significantly alter the cure rate. To return to the analogy with the newer forms of insulin, no more diabetic persons have had the disease controlled, although the control has been rendered simpler, safer and more precise. Accordingly, in the present discussion it is proposed to consider potentialities and indications rather than to present any detailed survey meticulously comparing five-year cure rates.

## CARCINOMA OF THE CERVIX

It remains true that the revival of interest in the surgical attack on carcinoma of the cervix has brought about a salvage rate equal to but no better than that achieved with irradiation therapy in comparable cases. The primary surgical attack, furthermore, is limited to League of Nations Stage I lesions and in most clinics only to a selected group of such patients. This leaves the majority of patients with carcinoma of the cervix that was invasive when first diagnosed committed to irradiation. The objectives

• At present, progress in the treatment of cancer consists of more extensive excision or more thorough irradiation.

The cure rate of pelvic cancer is proportionate not so much with the form of therapy used as with the stage of the disease when first diagnosed.

Any woman who consults a physician should have a pelvic examination regardless of the presence or absence of pelvic symptoms.

of such therapy are to produce an even blanket of irradiation across the pelvis, achieving a cancerocidal dose at all points. It is of importance to restate this objective only because over the years there has so often been a tendency to slip into the habit of administering intensive irradiation to the cervix and the immediate paracervical region, and to administer inadequate therapy to the lateral pelvic walls. The lateral wall is the first site of spread of cervical carcinoma, and cervical carcinoma is a lesion that is always further ahead of us than we think. Individual modalities of treatment are less important than this over-all objective of cancerocidal doses at all points; and against this objective each technique should be evaluated.

The weapons available include first of all x-ray for external therapy, and here the pattern of our thinking has been changed most significantly by the introduction of the supervoltage forms—the two million volt tube or the Van der Graf accelerator. There can be little doubt, reviewing the preliminary reports of the results of such therapy in gynecologic malignant disease, that the skin-sparing action associated with the increased voltage levels is a definite benefit. At present in the gynecologic clinic of Western Reserve University School of Medicine, external therapy which formerly delivered between 3,500 and 4,000 roentgens to the midpelvic plane is now delivering between 4,500 and 5,000 roentgens uniformly across the midpelvis. It must be acknowledged, however, that this skin-sparing benefit is perhaps less impressive with regard to the pelvic lesions than in those of the chest or neck, for as the dosage to the midpelvic level increases, the morbidity in the other pelvic viscera likewise increases. In patients observed by the author, bowel morbidity has been the most conspicuous change and has shown an increase of at least 25 per cent with the increased dosage level. In place of the top limitation imposed by skin tolerance, top limitation imposed by

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the patients' general systemic tolerance and by the local bowel reactions to these dosages are now not infrequently encountered.

The ability to increase the dosage to the side wall by 1,000 to 1,500 roentgens, however, has sharply limited the need for the other techniques which have been employed to raise the dosage in the nodal region. Thus the interstitial colloidal gold sponsored by Sherman and the nylon thread technique for the use of cobalt are perhaps less necessary with the approach to therapy available.

#### **Radium**

Radium remains the standby for central pelvic therapy and for achieving the high dosages to the cervix itself and to Point A. There has undoubtedly been a rise in recent years in the interstitial use of radium, and modifications of the Corscaden pattern are frequent. Much of this has been achieved by a reduction of the intensity of the individual sources, thus reducing the immediate reaction and necrosis around each needle, while relying on the crossfire of the various needles to create a field of adequate intensity within the fire pattern. In such circumstances the dosage delivered to the neighboring structures falls off sharply outside the pattern.

#### **Cobalt**

Cobalt<sup>60</sup> as a therapeutic weapon is undoubtedly here to stay in one form or another. It has a half life of 5.3 years and emits two gamma rays of 1.1 and 1.4 million electron volts intensity. It has an exceedingly weak beta ray, and heavy shielding to guard against beta-ray damage is not necessary. It is insoluble and inert if it should come in contact with body fluid or tissues, it can be activated in any desired shape, and it remains relatively inexpensive.

Radioactive cobalt has found its principal therapeutic application in two quite distinct forms. The first of these is the cobalt bomb—a mass of activated cobalt held in a special unit which directs the beam of the gamma rays much as x-rays would be directed from a therapy machine. In this form cobalt is used as a substitute for x-ray and studies of its gamma ray strength as compared to the output of a two million volt x-ray tube would indicate that the two are approximately equivalent. In other words the cobalt bomb can be considered as the roentgenologic equivalent of a supervoltage x-ray machine of a two million volt equivalent dosage level. It will have all of the drawbacks of external supervoltage and all of the advantages of such therapy. It will need periodic reactivation and has the technical disadvantage that it is emitting its beam all the time, whereas the x-ray tube is emitting its beam only when it is turned on.

Cobalt<sup>60</sup> has also been used as a radium substitute in various modalities for transvaginal application. When it is used in this way, the particularly attrac-

tive features are the ease in handling it and the lack of necessity for heavy filtration to remove the beta ray. Gone is the concept of the platinum and gold filters necessary with radium; containers of extraordinary fineness can be employed. Not only has it been used in colpostat and tandem therefore, but, with the advantage of these characteristics, has received considerable attention for various forms of interstitial therapy. The light aluminum needle which can be trimmed in length to suit the needs of the pelvis and the tumor distribution; the steel needle which in bulk is considerably smaller than the equivalent radiation strength of radium, or even the encasement of the cobalt portions in nylon tubing to be sewn into the tumor—these are examples of advantages in interstitial therapy.

#### **Gold**

Au<sup>198</sup> has properties that are quite distinct from cobalt. It has a half life of only 2.7 days, which immediately complicates the problem of getting the irradiated material from the reactor to the patient without loss of too much strength. For an institution to "keep gold on hand" in the same way that it can keep cobalt readily available is virtually impossible, since at the end of a week to ten days the strength of any given lot, so far as effectiveness is concerned, is completely gone. Radioactive gold emits but one gamma ray which is of a low degree of penetrability, and a beta ray with a high electron voltage spectrum. In its colloidal form it is relatively easily handled, it is inert in the body tissues, is insoluble, and can be activated in considerable quantities without significant cost.

Sherman and co-workers suggested the direct injection of Au<sup>198</sup> into the paracervical regions for treatment of cervical carcinoma. The colloidal particles are picked up by the lymphatic chains of the area and carried to the lateral pelvic walls, where the nodes concentrate the multiple sources of irradiation. That it can effectively alter the nodes morphologically has been demonstrated, but it still remains true that the physics of this type of therapy is of necessity approximate. With the half life declining rapidly as the sources of irradiation move toward their ultimate goal, and with the tissue volume being treated not completely known, any calculation of tissue roentgens delivered must be at best an educated guess. These difficulties may well be overcome, but at present the interstitial injection of radioactive colloidal gold in the therapy of carcinoma of the cervix remains a matter for study rather than for wide application.

#### **CARCINOMA OF THE FUNDUS AND CORPUS OF THE UTERUS**

In sharp contrast to the situation with carcinoma of the cervix, the primary attack on fundal carci-

noma remains surgical. Radiation therapy finds its place either for therapy of inoperable lesions where a full course treatment must be given around the pelvis and within the uterus, or as a preliminary to hysterectomy. The motives for such presurgical treatment by intercavitary irradiation are not always easy to define. Since the tumor can implant by direct seeding, probably the greatest benefit that is achieved by pretreatment with sources of radiation is to render the malignant cells temporarily incapable of such implantation and thereby reduce the risk of local seeding at the time of hysterectomy.

It is important to define the motive for this presurgical radiation therapy because it will influence both the dosage schedules and the forms of therapy employed. If the foregoing statement of motives is an accurate postulation of the reasoning behind the pre-hysterectomy therapy with intercavitary irradiation, then it should be possible to reduce the dosages significantly provided radiation is distributed uniformly within the uterus. Thus, Kotmeyer advocated a considerably smaller dosage of irradiation for fundal carcinoma than that customarily used in this country, and it is probable that delivering 1,200 roentgens at 0.5 cm. distance beneath the endometrial surface should be sufficient to achieve such an objective. The one prerequisite for such a dosage schedule would be a uniform application of the irradiation throughout the uterine cavity, and this can be achieved only by multiple sources packed within the uterus. The traditional application of a tandem of radium for a given number of "milligram hours" leads to local areas of sharp overdosage and other areas of pronounced undertreatment. Undoubtedly in some areas of the uterine cavity the desideratum of rendering the cells at least sick enough that they will not implant readily is more than successfully achieved, whereas in other areas the dosage is woefully inadequate for such a purpose.

In this connection Hendricks suggested the use of multiple cobalt sources in the form of beads which are strung together for packing into the uterine cavity. These can follow the contours of the most irregular uterus, giving an even field of irradiation over the entire endometrial surface. By using an inactive chain for preliminary packing and measurement of the capacity of the uterus, the total length of time that the operative team is exposed to irradiation is considerably reduced and this technique should improve the multiple source therapy of fundal carcinoma prior to hysterectomy.

#### CARCINOMA OF THE OVARY

Radiation therapy has no actual or logical place in the primary treatment of carcinoma of the ovary. It remains tragically true, however, that in so many

cases ovarian carcinoma has already penetrated the capsule of the tumor and implanted metastatically on the peritoneal surfaces at the time of the primary surgical attack that palliative irradiation remains necessary for the ultimate management of the patient. Since the area involved is so great, external sources of radiation—either from x-ray tube or from the cobalt bomb—usually render the patient exceedingly ill systemically without being able to achieve a cancerocidal dose at the midabdominal plane. For this reason, many efforts have been made to find a substitute for external x-ray therapy of metastatic ovarian carcinoma.

The intraperitoneal administration of radioactive colloidal gold is one of the best known of these attempts to palliate patients who have ascites and multiple peritoneal implants. It must be borne in mind that in these circumstances gold is not employed for its gamma ray therapy. Actually, the penetrability of the gamma ray is such that when the solution bathes the outside of the intestinal tract there are no evidences of mucosal burns inside the tract. With such minimal penetrability for the gamma rays (actually about 0.4 mm.) delivery of a cancerocidal dose of gamma roentgens into tumor nodules of any size cannot be expected. Actually, of course, in such a situation colloidal gold is being employed for its beta ray therapy. The strong beta ray burns the peritoneal surface, sclerosing it and reducing its ability to form ascitic fluid. This is palliation in its purest sense, but not to any degree therapy. The tumor continues to grow unabated and uncontrolled.

It would seem sensible, if the purpose of the gold here is to use its beta ray, to employ a pure beta emitter so that the gamma ray would present no problem at all. For this reason  $P_{32}$  was suggested, and experiments were carried out with chromic phosphate. In a few cases in which it was possible to obtain nodes from patients who had received this material intraperitoneally, however, as much as 20 per cent was accounted for outside the peritoneal cavity in nodal tissue or in bone, indicating some breakdown of the material.

It is impossible to conclude such a topic as this without two important reminders:

In the first place the topic of discussion here is new modalities in the treatment of gynecologic malignant disease, and it is well to remember that progress in treatment has nothing to do with progress in approaching the cure of cancer. At present, progress in the treatment of carcinoma consists of cutting it out more extensively or burning it more thoroughly. Neither of these implies, in any sense curative measures; and the cure of carcinoma will,

in all probability, be biochemical rather than radiologic.

The second point is, of course, that the cure rate of all of the lesions mentioned is, in the last analysis, proportionate not so much to the form of therapy employed as to the stage of the disease process when it is first diagnosed. The best means of radiologic treatment and the most skillful roentgen therapist remain earthbound by the clinical stage which the neoplasm has reached at the time treatment is started. To have any significant impact upon the national salvage rate for the gynecologic malignant diseases, we must diagnose them earlier. This means, for physicians, a high index of suspicion, an intelligent use of the diagnostic aids which are currently available and an increasing practice of prophylactic gynecology.

No therapy is any better than the diagnosis that precedes it, just as no diagnostic aid has been invented for the patient who stays at home. From the point of view of the physician, it is impossible to discharge a woman from one's practice; she must be given not a dismissal, but rather a return appointment.

Finally, the presence or absence of pelvic symptoms should have nothing to do with determining which patient should have a pelvic examination. If the patient has a pelvis and reaches the office, she should have a pelvic examination. This should be a universal rule—even if it subsequently turns out that she has come only to collect money for the Community Chest.

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